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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,649	05/23/2001	Julian M.C. Golec	VPI/00-114	1044

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EXAMINER	
RUSSEL, JEFFREY E	

ART UNIT	PAPER NUMBER
1654	11

DATE MAILED: 02/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/863,649	Applicant(s) GOLEC, JULIAN M.C.	
	Examiner Jeffrey E. Russel	Art Unit 1654	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7-9 and 11-17* is/are rejected.

7)☒ Claim(s) *3-6 and 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. The Sequence Listing filed December 13, 2002 has been approved.

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> It does not identify the city and either state or foreign country of residence of each inventor. The residence information may be provided on either on an application data sheet or supplemental oath or declaration.

The declaration filed November 28, 2001 does not provide a city of residence for inventor Golec.

3. Claims 1, 2, 7-9, and 11-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The definition of R^1 in claims 1 and 8 is unclear because it is not clear what structure a CHN_2 group has. It is not even clear that this is a monovalent group, as required by formula I. The definition of R^3 in claims 1 and 8 is unclear because formula I requires R^3 to be a monovalent group; however, one of the listed possibilities, F_2, is the formula for elemental fluorine and is not a monovalent group. Claims 2 and 9 are unclear because it appears that feature (d) of each claim is automatically satisfied by the definition of Ar in the independent claims. Claims 7 and 11 are indefinite because of their incorporation by reference of the compounds listed in Table 1. Claims are to be complete in and of themselves, and Applicants have not demonstrated that there is no other practical way to claim the invention, e.g., by explicitly reciting the compound structures in the claims. See MPEP 2173.05(s). At claim 12, page 86, line 28, the phrase "various forms of liver disease including" is unclear as to whether the scope of the claim is to be limited to particular liver diseases or if the claim

embraces the treatment of all liver diseases which can be alleviated by treatment with a caspase inhibitor. It is recommended that the phrase be amended to read "liver disease,". Claims 14 and 15 are indefinite because of the use of the term "derivative". It is not clear what degree of functional and/or structural similarity a substance must have with the compounds of formula I in order for the substance to be considered a "derivative" of the compounds of formula I. The term "derivative" is not defined in Applicant's specification, nor does it have any art-accepted meaning.

4. Claim 12 is objected to because of the following informalities: At claim 12, page 86, line 27, "or" should be deleted. Appropriate correction is required.

5. Claims 14 and 15 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 14 and 15 are broader in scope than the independent claim upon which they depend, because the independent claim is limited to the use of compounds of formula I, whereas dependent claims have been expanded to include the use of pharmaceutically acceptable derivatives of compounds of formula I. Claims 14 and 15 are broader in scope than the independent claim upon which they depend, because the independent claim is limited to the in vivo administration of a compound of formula I to a mammal, whereas dependent claim 14 embraces ex vivo and/or in vitro cell cultures, and dependent claim 15 embraces ex vivo and/or in vitro preservation of blood products.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

7. Claims 1, 2, 8, 9, 12, 16, and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Ohmoto et al (U.S. Patent No. 6,136,834). Ohmoto et al teach compounds in Examples 18(23), 18(24), 19(21), and 19(22) which meet the requirements of Applicant's formula I in which R^1 is R which is a substituted aliphatic group or a substituted heterocyclylalkyl group. The compounds of Ohmoto et al are ICE inhibitors which are used to treat diseases such as infectious diseases, Alzheimer's disease, AIDS, leukemia, and neoplasm. See, e.g., column 219, line 10 - column 220, line 59; column 414, line 37 - column 415, line 21; column 422, line 42 - column 423, line 26; and claims 13-14. These compounds of Ohmoto et al are also deemed to constitute pharmaceutically acceptable derivatives of the other compounds embraced by Applicant's formula I in view of their structural and functional similarity.

8. Claims 13-15 are rejected under 35 U.S.C. 103(a) as being obvious over Ohmoto et al (U.S. Patent No. 6,136,834) as applied against claims 1, 2, 8, 9, 12, 16, and 17 above, and further in view of Hagmann et al (U.S. Patent No. 5,866,545) and Baust et al (U.S. Patent No. 6,045,990). Ohmoto et al do not teach using their ICE inhibitors to treat complications associated with coronary artery bypass grafts, or to preserve cells, organs to be transplanted, or blood products. Hagmann et al disclose the use of ICE inhibitors to treat graft rejection and graft-versus-host disease (see, e.g., column 2, lines 38-54). Baust et al disclose the use of caspase protease inhibitors to treat animal or human organs, tissues or cells for hypothermic storage, e.g., prior to transplantation (see, e.g., column 5, lines 58-61; column 16, lines 36-54; and claim 6). It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use the ICE inhibitors of Ohmoto et al to treat complications associated with coronary artery bypass grafts, or to preserve cells, organs to be transplanted, or blood products, because Hagmann et al and Baust et al teach that these are known uses for ICE inhibitors; because the ICE inhibitors of Ohmoto et al are structurally and functionally analogous to those described by Hagmann et al and Baust et al; because it is the ability to inhibit ICE, rather than the presence of any particular chemical structure, which would have been expected to be necessary in order to treat graft rejection and graft-versus-host disease as taught by Hagmann et al or to treat animal or human organs, tissues or cells for hypothermic storage as taught by Baust et al; and because it is prima facie obvious to use ICE inhibitors or caspase inhibitors for the same pharmaceutical purposes that other ICE inhibitors and caspase inhibitors are used.

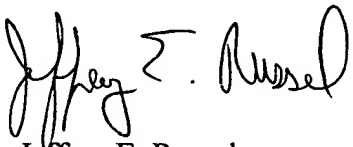
9. Claims 3-6 and 10 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base

claim and any intervening claims. Claims 7 and 11 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims. The prior art of record does not teach or suggest compounds having the structures recited in instant claims 3-7, 10, and 11. In particular, note that Ohmoto et al, applied above, do not teach or suggest the R^1 group required by instant claims 3-7, 10, and 11. Accordingly, methods of using these compounds are also novel and unobvious over the prior art of record.

It is recognized that there is a WO equivalent to Ohmoto et al (U.S. Patent No. 6,136,834) applied above, and that the equivalent has an earlier publication date than the U.S. patent. However, WO Patent Application 97/24339 is over 1000 pages in length and is not in the English language, and therefore the examiner does not believe it is useful to cite or apply this reference at this time. If the date of Applicant's invention becomes an issue during prosecution, the examiner will re-consider the need to apply the WO Patent Application '339. Any new rejection based upon the WO Patent Application '339 will result in a non-final Office action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

February 5, 2003